112, second paragraph, as allegedly indefinite. Claims 1-4, 6-8, 10-13, 15, and 40-43 have been rejected under 35 U.S.C. § 102 (e) as allegedly anticipated by U.S. Patent No. 5,830,755. Reconsideration of the objection and rejections is hereby requested.

The Amendments to the Claims

Claims 9, 14, and 16-39 have been cancelled as drawn to non-elected inventions. Claims 2, 13, and 42 also have been cancelled. Applicants reserve the right to pursue any cancelled subject matter in a continuation, continuation-in-part, divisional, or other application. Cancellation of any subject matter should not be construed as abandonment of that subject matter. Claims 1, 12, 40, and 41 have been amended to recite that the strong antigen is an allogeneic agent as supported by the specification at, for instance, page 11, lines 3-12, page 51 (originally-filed claim 2), page 52 (originally-filed claim 13), and page 55 (originally-filed claim 42). Claim 12 also has been amended to recite "wherein the lymphocyte is activated *in vivo* with the strong antigen." Claim 15 has been amended to delete the term "donor" to point out clearly and claim distinctly the present invention. No new matter has been added by way of these amendments. Separate documents setting forth the precise changes to the claims, as well as the text of all pending claims, are enclosed herewith.

Discussion of the Objection to the Specification

The Office has objected to the specification, as the status of U.S. Patent Application No. 08/547,263, which is cited on page 17, line 2, allegedly needs to be updated. However, according to the U.S. Patent and Trademark website, this patent application is on appeal and, therefore, the specification of the instant patent application does not need to be updated at the present time. In view of the foregoing, Applicants request that the objection to the specification be withdrawn.

Discussion of the Rejection under U.S.C. § 112, second paragraph

Claims 1-4, 6-8, 10-13, 15, and 40-43 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. This rejection is traversed for the reasons set forth below.

The Office argues that the term "preselected" is allegedly unclear. However, the meaning of the term "preselected" is exemplified throughout the specification and, in particular, at page 17, lines 12-25. Specifically, the specification states "[i]n one embodiment, the specific expansion step amplifies an individual or a subpopulation of T cells whose endogenous TCR is directed to the strong antigen(s) used to expand the T

cells. In this way, T cells which react with the antigen(s) are selected out and amplified from a mixed population of T cells originally obtained from the patient...These preselected...T cells are introduced into a patient." The meaning of the term "preselected" is further demonstrated through Examples 7 and 8 in which it is disclosed that human peripheral blood mononuclear cells (PBMC) isolated from one donor were preselected for reactivity against human PBMC from another donor.

The Office alleges that the metes and bounds of the term "strong antigen" cannot be determined, as it allegedly is not defined in the specification and allegedly does not have an art-accepted meaning (page 6 of Paper No. 13). However, this phrase is, in fact, defined in the specification at, for instance, page 11, lines 3-7, and page 18, lines 15-16. A strong antigen is an antigen capable of inducing proliferation of preselected adoptively transferred T cells. Examples of strong antigens include alloantigens and viral agents. Also, a strong antigen is recognized by the endogenous T cell receptor of a dual specificity lymphocyte.

The Office contends that the meaning of the term "allogeneic agent" cannot be ascertained, as this phrase allegedly is not defined in the specification and allegedly does not have an art-accepted meaning. However, "allogeneic agent" is defined in the specification at, for example, page 11, lines 7-8. Allogeneic agents include allogeneic tissues, allogeneic cells, and allogeneic proteins. Allogeneic agents are a specific type of strong antigen. Furthermore, the meaning of this term is exemplified in Examples 7 and 8, wherein the allogeneic agents that stimulated the human PBMC were human PBMC isolated from a human donor that is different from the donor from which the stimulated PBMC were isolated, e.g., the PBMC of Donor 410 were stimulated with the PBMC of Donor 556, which were the allogeneic agents.

The Office further states that the term "derived" is unclear in the context of claim 4. However, in view of the definition of "tumor antigen," which is found in the specification at, for instance, page 13, lines 19-26, one of ordinary skill in the art can determine the meaning of this term. Specifically, "a tumor antigen that is derived from ovarian cancer" is a tumor antigen that is only found on a tumor, one that is expressed on tumor cells and has limited expression on normal tissue, or one that is over-expressed on tumor cells as compared to the expression on a variety of normal tissues, wherein the tumor or tumor cells are of ovarian cancer.

The Office also contends that the term "Mov-γ" in claim 10 is allegedly unclear. However, this term is understood by one of ordinary skill in the art, as this chimeric receptor is described in Hwu et al., *J. Exp. Med.* 178: 361-366 (1993), and Hwu et al., *Cancer Res.* 55: 3369-3373 (1995), both of which are cited in the specification at, for

instance, page 27, lines 4-7, and both of which are incorporated by reference into the instant patent application. From the abstract of Hwu et al., *Cancer Res.* 55: 3369-3373 (1995) alone, it is apparent that the term " Mov-γ" refers to a chimeric receptor derived from the monoclonal antibody Mov18, which binds to a folate-binding protein overexpressed on most human ovarian adnocarcinomas.

The Office further argues that the phrase "can be activated *in vivo* with the strong antigen" recited in claim 12 is allegedly unclear. However, in view of the amendment to the claim, this point of rejection is believed to be moot.

The Office alleges that the term "donor" in claim 15 is purportedly unclear. However, in view of the amendment to the claim, this point of rejection is believed to be moot.

The Office contends that the term "dual specificity lymphocytes" in claim 41 is allegedly indefinite. However, this term is defined in the specification at, for example, page 11, lines 19-21. Furthermore, the meaning of this term is demonstrated throughout the specification, e.g., page 30, lines 8-10, page 34, lines 6-8, and Figure 1.

The Office also contends that the term "folate binding protein" is allegedly unclear. However, the specification teaches at, for instance, page 30, 2nd and 3rd lines from the bottom, that FBP is a gene that is highly expressed on ovarian adenocarcinomas.

Applicants point out that claims 2, 13, and 42 have been cancelled, such that the rejection with respect to these claims is moot. In view of the foregoing, all of the pending claims meet the requirements of 35 U.S.C. § 112, second paragraph. Therefore, Applicants request that this rejection be withdrawn.

Discussion of the Rejection under U.S.C. § 102(e)

Claims 1-4, 6-8, 10-13, 15, and 40-43 have been rejected under 35 U.S.C. § 102 (e) as allegedly anticipated by U.S. Patent No. 5,830,755 (the '755 patent). Specifically, the Office contends that the '755 patent teaches TIL transfected with an Mov-γ. Also, the Office argues that the present invention is inherent to the TILs of the '755 patent, since they have an endogenous T-cell receptor reactive with a strong antigen, since they were stimulated *in vitro* with antigen and since the term "strong antigen" is allegedly unclear. This rejection is traversed for the reasons set forth below.

Contrary to what the Office asserts, the present inventive lymphocytes and compositions comprising the same are different from those of the '755 patent in that the present inventive lymphocytes were preselected with a *strong* antigen; i.e., selected out of a mixed population based upon the ability to react to a *strong* antigen (emphasis added). As stated on page 11, lines 3-6, a "strong antigen" is "an antigen capable of inducing

proliferation of preselected adoptively transferred T cells." Although the TIL of the '755 patent were "antigen-stimulated," the '755 patent does not teach that the antigen was a "strong antigen," i.e., that the antigen induced proliferation.

In order to advance prosecution and not in acquiescence of the rejection, however, claims 1, 12, and 41 have been amended to incorporate the features of claims 2, 13, and 42, respectively, and claim 40 has been amended to recite that the strong antigen is an allogeneic agent. Also, claims 2, 13, and 42 have been cancelled. As the '755 patent does not teach the use of an allogeneic agent as an antigen, the '755 cannot be said to teach each and every element of the claimed invention.

In view of foregoing, the '755 patent cannot be said to anticipate the present invention. Therefore, Applicants hereby request that the rejection under Section 102(e) be withdrawn.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

Carol Larcher, Reg. No. 35,243
One of the Attorneys for Applicant
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: June 2, 2003
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CERTIFICATE OF MAILING

I hereby certify that this AMENDMENT AND RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date: June 2, 2003

Murilla Gallegos